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CONTENTS/SUMMARIES

- Bacillus subtilis* Sporulation: Regulation of Gene Expression and Control of Morphogenesis.** Jeffery Errington 1-33

Summary: Bacillus subtilis sporulation is an adaptive response to nutritional stress and involves the differential development of two cells. In the last 10 years or so, virtually all of the regulatory genes controlling sporulation, and many genes directing the structural and morphological changes that accompany sporulation, have been cloned and characterized. This review describes our current knowledge of the program of gene expression during sporulation and summarizes what is known about the functions of the genes that determine the specialized biochemical and morphological properties of sporulating cells. Most steps in the genetic program are controlled by transcription factors that have been characterized in vitro. Two sporulation-specific sigma factors, σ^E and σ^F , appear to segregate at septation, effectively determining the differential development of the mother cell and prespore. Later, each σ is replaced by a second cell-specific sigma factor, σ^K in the mother cell and σ^G in the prespore. The synthesis of each sigma factor is tightly regulated at both the transcriptional and posttranslational levels. Usually this regulation involves an intercellular interaction that coordinates the developmental programmes of the two cells. At least two other transcription factors fine tune the timing and levels of expression of genes in the σ^E and σ^K regulons. The controlled synthesis of the sigma factors and other transcription factors leads to a spatially and temporally ordered program of gene expression. The gene products made during each successive stage of sporulation help to bring about a sequence of gross morphological changes and biochemical adaptations. The formation of the asymmetric spore septum, engulfment of the prespore by the mother cell, and formation of the spore core, cortex, and coat are described. The importance of these structures in the development of the resistance, dormancy, and germination properties of the spore is assessed.

- Meningococcal Lipopolysaccharides: Virulence Factor and Potential Vaccine Component.** A. F. M. Verheul, H. Snippe, and J. T. Poolman 34-49

Summary: Lipopolysaccharides (LPS) are surface components of the outer membrane of Neisseria meningitidis. Today, 12 different types of meningococcal LPS (immunotypes) are known, of which 3 are prevalent in the western world. The differences between these immunotypes are in the oligosaccharide part of the LPS molecule and consist of small differences in the oligosaccharide structure, the amount and location of phosphoethanolamine groups, and the degree of O acetylation of individual monosaccharides. Although the differences between the various immunotypes are small, they have a profound influence on the immunochemical and immunological properties of these molecules. Furthermore, each individual strain synthesizes a number of different

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LPS molecules. The expression of the various components (protective epitopes) is influenced by growth conditions and growth phase. Meningococci can endogenously sialylate their LPS, which constitutes one of the mechanisms by which N. meningitidis can evade the response of the human host. Meningococcal LPS play a key role in the induction of septic shock and can probably enhance the invasiveness of meningococcal strains and shield protective epitopes. Therefore, incorporation of (detoxified) LPS or oligosaccharide components derived therefrom might be very beneficial for the efficacy of a vaccine against group B meningococci. An overview of the development of vaccines against group B meningococci is given, and the status and potential of meningococcal LPS-derived (synthetic) oligosaccharide-protein conjugate vaccines are discussed.

The Complete General Secretory Pathway in Gram-Negative Bacteria.

Anthony P. Pugsley.....

50-108

Summary: The unifying feature of all proteins that are transported out of the cytoplasm of gram-negative bacteria by the general secretory pathway (GSP) is the presence of a long stretch of predominantly hydrophobic amino acids, the signal sequence. The interaction between signal sequence-bearing proteins and the cytoplasmic membrane may be a spontaneous event driven by the electrochemical energy potential across the cytoplasmic membrane, leading to membrane integration. The translocation of large, hydrophilic polypeptide segments to the periplasmic side of this membrane almost always requires at least six different proteins encoded by the sec genes and is dependent on both ATP hydrolysis and the electrochemical energy potential. Signal peptidases process precursors with a single, amino-terminal signal sequence, allowing them to be released into the periplasm, where they may remain or whence they may be inserted into the outer membrane. Selected proteins may also be transported across this membrane for assembly into cell surface appendages or for release into the extracellular medium. Many bacteria secrete a variety of structurally different proteins by a common pathway, referred to here as the main terminal branch of the GSP. This recently discovered branch pathway comprises at least 14 gene products. Other, simpler terminal branches of the GSP are also used by gram-negative bacteria to secrete a more limited range of extracellular proteins.

Protein Secretion in Bacillus Species.

Marjo Simonen and Ilkka

Palva.....

109-137

Summary: Bacilli secrete numerous proteins into the environment. Many of the secretory proteins, their export signals, and their processing steps during secretion have been characterized in detail. In contrast, the molecular mechanisms of protein secretion have been relatively poorly characterized. However, several components of the protein secretion machinery have been identified and cloned recently, which is likely to lead to rapid expansion of the knowledge of the protein secretion mechanism in Bacillus species. Comparison of the presently known export components of Bacillus species with those of Escherichia coli suggests that the mechanism of protein translocation across the cytoplasmic membrane is conserved among gram-negative and gram-positive bacteria; differences are found in steps preceding and following the translocation process. Many of the secretory proteins of bacilli are produced industrially, but several problems have been encountered in the production of Bacillus heterologous secretory proteins. In the final section we discuss these problems and point out some possibilities to overcome them.

Molecular Genetics of Aminoglycoside Resistance Genes and Familial Relationships of the Aminoglycoside-Modifying Enzymes.

K. J. Shaw, P. N. Rather, R. S. Hare, and G. H. Miller....

138-163

Summary: The three classes of enzymes which inactivate aminoglycosides and lead to bacterial resistance are reviewed. DNA hybridization studies have shown that different genes can encode aminoglycoside-modifying enzymes with identical resistance profiles. Comparisons of the amino acid sequences of 49 aminoglycoside-modifying enzymes have revealed new insights into the evolution and relatedness of these proteins. A

preliminary assessment of the amino acids which may be important in binding aminoglycosides was obtained from these data and from the results of mutational analysis of several of the genes encoding aminoglycoside-modifying enzymes. Recent studies have demonstrated that aminoglycoside resistance can emerge as a result of alterations in the regulation of normally quiescent cellular genes or as a result of acquiring genes which may have originated from aminoglycoside-producing organisms or from other resistant organisms. Dissemination of these genes is aided by a variety of genetic elements including integrons, transposons, and broad-host-range plasmids. As knowledge of the molecular structure of these enzymes increases, progress can be made in our understanding of how resistance to new aminoglycosides emerges.

Ether Polar Lipids of Methanogenic Bacteria: Structures, Comparative Aspects, and Biosyntheses. Yosuke Koga, Masateru Nishihara, Hiroyuki Morii, and Masayo Akagawa-Matsushita ...

164-182

Summary: Complete structures of nearly 40 ether polar lipids from seven species of methanogens have been elucidated during the past 10 years. Three kinds of variations of core lipids, macrocyclic archaeol and two hydroxyarchaeols, were identified, in addition to the usual archaeol and caldarchaeol (for the nomenclature of archaeal [archaeobacterial] ether lipids, see the text). Polar head groups of methanogen phospholipids include ethanolamine, serine, inositol, N-acetylglucosamine, dimethyl- and trimethylaminopentane-2,3,6-triol, and glucosaminylinositol. Glucose is the sole hexose moiety of glycolipids in most methanogens, and galactose and mannose have been found in a few species. Methanogen lipids are characterized by their diversity in phosphate-containing polar head groups and core lipids, which in turn can be used for chemotaxonomy of methanogens. This was shown by preliminary simplified analyses of lipid component residues. Core lipid analysis by high-pressure liquid chromatography provides a method of determining the methanogenic biomass in natural samples. There has been significant progress in the biosynthetic studies of methanogen lipids in recent years. In vivo incorporation experiments have led to delineation of the outline of the synthetic route of the diphytanylglycerol ether core. The mechanisms of biosynthesis of tetraether lipids and various polar lipids, and cell-free systems of ether lipid synthesis, however, remain to be elucidated. The significance and the origin of archaeal ether lipids is discussed in terms of the lipid composition of bacteria living in a wide variety of environments, the oxygen requirement for biosynthesis of hydrocarbon chains, and the physicochemical properties and functions of lipids as membrane constituents.

Pathogenesis of Human Immunodeficiency Virus Infection. Jay A. Levy

183-289

Summary: The lentivirus human immunodeficiency virus (HIV) causes AIDS by interacting with a large number of different cells in the body and escaping the host immune response against it. HIV is transmitted primarily through blood and genital fluids and to newborn infants from infected mothers. The steps occurring in infection involve an interaction of HIV not only with the CD4 molecule on cells but also with other cellular receptors recently identified. Virus-cell fusion and HIV entry subsequently take place. Following virus infection, a variety of intracellular mechanisms determine the relative expression of viral regulatory and accessory genes leading to productive or latent infection. With CD4⁺ lymphocytes, HIV replication can cause syncytium formation and cell death; with other cells, such as macrophages, persistent infection can occur, creating reservoirs for the virus in many cells and tissues. HIV strains are highly heterogeneous, and certain biologic and serologic properties determined by specific genetic sequences can be linked to pathogenic pathways and resistance to the immune response. The host reaction against HIV, through neutralizing antibodies and particularly through strong cellular immune responses, can keep the virus suppressed for many years. Long-term survival appears to involve infection with a relatively low-virulence strain that remains sensitive to the immune response, particularly to control by CD8⁺ cell antiviral activity. Several therapeutic approaches have been attempted, and others are under investigation. Vaccine development has provided some encouraging results, but the observations indicate the major challenge of preventing infection by HIV. Ongoing research is necessary to find a solution to this devastating worldwide epidemic.

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ERRATUM

Bacteriophage Lambda as a Cloning Vector.

Vijay M. Chauthaiwale, A. Therwath, and Vasanti V.
Deshpande

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